loop devices for blood glucose control in normal and diabetic subjects. Diabetes 1979 Jan; 28:71-81
7. Schade DS, Eaton RP, Edwards WS, et al: A remotely programmable insulin delivery system—Successful short-term implantation in man. JAMA 1982 Apr 2; 247:1848-1853
8. Irsigler K, Kritz H, Hagmuller G, et al: Long-term continuous intraperitoneal insulin infusion with an implanted remote-controlled insulin infusion device. Diabetes 1981 Dec; 30:1072-1075
9. Mirouze J, Selam JL: Clinical experience in human diabetics with portable and implantable insulin minipumps. Life Support Systems 1983 Jan; 1:39-50
10. Eaton RP, Allen RC, Schade DS, et al: Prehepatic insulin production in man: Kinetic analysis using peripheral connecting peptide behavior. J Clin Endocrinol Metab 1980 Mar; 51:520-528
11. Standefer JC, Eaton RP: Evaluation of a colorimetric method for determination of glycosylated hemoglobin. Clin Chem 1983 Jan; 29:135-140
12. Unger RH: Meticulous control of diabetes: Benefits, risks, and precautions. Diabetes 1982 Jun; 31:479-483
13. Schade DS, Eaton RP: The peritoneum—A potential insulin delivery route for a mechanical pancreas. Diabetes Care 1980 Mar-Apr; 3:229-234
14. Schade DS, Santiago JV, Skyler JS, et al: Intensive Insulin Therapy. Princeton, NJ, Excerpta Medica, 1983, pp 129-148

Enterococcal Endocarditis Following Flexible Sigmoidoscopy

WILMER RODRIGUEZ, MD
JOEL S. LEVINE, MD
Denver

THE ASSOCIATION BETWEEN lower gastrointestinal (GI) tract endoscopy and bacteremia has been controversial. Studies have shown an incidence of bacteremia following sigmoidoscopy or colonoscopy of 10% to 27%,[1-3] whereas some report that bacteremia occurs in a negligible portion[4,5] or not at all.[6-9] Because of these conflicting data and the absence of a reported case of endocarditis after a lower GI tract procedure, the American Heart Association (AHA) suggested in 1977 that antibiotic prophylaxis be given only for lower GI tract procedures in patients who have prosthetic heart valves.[10] In a recent nationwide survey of endoscopy program directors, however, most did not recommend antibiotic prophylaxis for lower GI tract procedures in any patient.[11] Whether either of these recommendations reflects actual practice habits is unknown.

We have recently become aware of a patient in whom enterococcal endocarditis developed following flexible sigmoidoscopy. We reviewed a local hospital's records and the medical literature for similar cases and surveyed endoscopists, cardiologists and infectious disease specialists in the Denver metropolitan area about their current recommendations for antibiotic prophylaxis in patients with various valvular lesions. In light of these findings, we examined the costs and possible benefits of providing antibiotic prophylaxis to patients with valvular heart disease.

Report of a Case

The patient, a 66-year-old man with compensated rheumatic heart disease (aortic regurgitation and mitral stenosis and regurgitation), was admitted to hospital with painless hematochezia of one day's duration. On that admission a flexible sigmoidoscopy (without biopsy) was done without antibiotic prophylaxis. Internal hemorrhoids were noted, but no bleeding source was identified. Because the bleeding had stopped spontaneously and hematocrit and coagulation values were normal, the patient was discharged in stable condition. Four days later fever, lethargy, generalized weakness and slurred speech developed. The next day the patient was transferred to Rose Medical Center (Denver).

On physical examination at the time of admission he had a temperature of 40°C (104°F). The patient was in a toxic state and was not oriented to place or time. There was no evidence of trauma, papilledema, Roth spots, conjunctival hemorrhages or neck rigidity. There were rales at both lung bases. Murmurs characteristic of aortic regurgitation, mitral stenosis and mitral regurgitation were present. The abdomen was not tender, there was no visceromegaly and a stool specimen was negative for occult blood. Examination of the extremities showed subungual splinter hemorrhages. On neurologic examination he had right upper extremity paresis, right arm and leg hyperreflexia and no pathologic reflexes.

On admission six blood specimens for culture were drawn and within 24 hours all cultures were positive for enterococci. Lumbar puncture showed no evidence of cerebrospinal fluid infection and therapy was immediately begun with ampicillin, 2 grams given intravenously every four hours, and gentamicin sulfate, 80 mg given intravenously every six hours. Subsequent computed tomographic scan of the head showed minimal cortical atrophy but no evidence of vascular or space-occupying lesions. As compared with a prior study, a two-dimensional echocardiogram showed increased echogenicity at the mitral valve that was felt to be vegetations. The patient became afebrile after four days of antibiotic therapy, and no evidence of a noncardiac focus of infection (abdominal, urinary or skin) was found. The patient's abnormal neurologic signs gradually resolved and he was discharged in good health after six weeks of therapy. He has remained well, without evidence of colonic disease.

Methods

After becoming aware of this case, we reviewed all charts at Rose Medical Center for the years 1979 through 1982 that had a discharge diagnosis of bacterial endocarditis. In addition, all records of patients having enterococci cultured from blood were reviewed for the same time period. Rose Medical Center was chosen because the index case was found at this hospital and because it had the highest volume of lower GI tract procedures (sigmoidoscopies and colonoscopies) among area hospitals.

Appreciating that a low frequency complication such as endocarditis would be unlikely to be found by simple chart review and wanting to judge what the current practice habits in the Denver metropolitan area were, we sent a questionnaire to local endoscopists (N=47), cardiologists (N=50) and infectious dis-

(Rodriguez W, Levine JS: Enterococcal endocarditis following flexible sigmoidoscopy. West J Med 1984 Jun; 140:951-953)

From the Division of Gastroenterology, Department of Medicine, University of Colorado School of Medicine, Denver.
This study was supported by the Kern Research Foundation.
Submitted, revised, November 9, 1983.
Reprint requests to Joel S. Levine, MD, Div of Gastroenterology, Mail Container B158, Univ of Colorado Health Sciences Center, 4200 E 9th Ave, Denver, CO 80262.

TABLE 1.—*Antibiotic Prophylaxis for Lower Gastrointestinal Tract Endoscopy—Practice Habits in the Denver Metropolitan Area, 1983*

Physician Specialties	Indications for Prophylaxis: Prosthetic Valves Only Percent	All Valvular Diseases Percent	Do Not Give Percent
Endoscopists (N=42)	21	50*	10
Cardiologists (N=36)	11	58	31
Infectious disease (N=10)	10	50*	30

*The remainder (19% of endoscopists and 10% of infectious disease specialists) give prophylaxis for all valvular disease, with the exception of either aortic stenosis or mitral valve prolapse.

ease specialists (N=15). The endoscopists were asked whether or not they query patients about or examine them for valvular heart disease before doing lower GI tract procedures. All physicians were asked whether or not they (1) "Recommend that antibiotic prophylaxis be given" to no patients who have valvular disease or to those who have any or all of the following: mitral stenosis, mitral regurgitation, aortic stenosis, aortic regurgitation, mitral valve prolapse or prosthetic heart valves; (2) give one, two or three doses of antibiotics if they do give prophylaxis, and (3) have ever encountered a case of endocarditis following a lower GI tract procedure. These responses were anonymous and no attempt was made to make certain that the physicians' practice conformed to these recommendations by doing a chart review.

Results

Chart Review

Between 1979 and 1982 there were 18 cases of bacterial endocarditis at Rose Medical Center, and in three cases the offending agent was an enterococcus. In only one case (the index case) could a lower GI tract procedure be temporally related. During the four years reviewed there were 22 cases of enterococcal bacteremia, and in only the index case could a lower GI tract procedure be implicated. A careful search of the medical literature was also unsuccessful in finding additional cases of endocarditis due to a lower GI tract endoscopy.

Physician Survey

The results of the survey of physicians are summarized in Table 1. In all, 42 of 47 endoscopists (89%), 36 of 50 cardiologists (72%) and 10 of 15 infectious disease specialists (67%) responded to the questionnaire. Almost all endoscopists (41 of 42) were concerned enough about this problem to ask about or to examine a patient for valvular heart disease immediately before doing lower GI tract endoscopy. Only a small minority of the physicians who responded would strictly follow the AHA guidelines of prophylactically treating only patients who had prosthetic valves (21%, 11% and 10% of endoscopists, cardiologists and infectious disease consultants, respectively). Most would give antibiotics prophylactically to patients with any type of valvular heart disease, including mitral valve prolapse. Very few endoscopists, but a third of the responding cardiologists and infectious disease specialists, would not give prophylaxis for lower GI tract endoscopic procedures. In light of these practice habits, it is interesting to note that none of the 88 physicians had seen or heard of a case of endocarditis following these procedures.

Of those physicians who would give antibiotic prophylaxis, only 42% of the endoscopists, 56% of the cardiologists and 43% of the infectious disease consultants would recommend the full three doses over 16 hours suggested by the AHA.[11] The remainder are evenly divided between giving one or two doses of antibiotics.

Discussion

We have presented what is probably the first reported case of enterococcal endocarditis following a lower GI tract endoscopic procedure. This happened in a man who had uncomplicated rheumatic heart disease, five days after an atraumatic flexible sigmoidoscopy without antibiotic prophylaxis. This short duration between exposure and endocarditis has been noted with virulent organisms such as enterococci. The neurologic symptoms, possible vegetations seen by cardiac ultrasound study and splinter hemorrhages strongly support the diagnosis of endocarditis. The enterococci strongly suggest a colonic source, with the endoscopy likely causing the initial bacteremia. As rigid or flexible sigmoidoscopy is more widely used to screen for curable colorectal neoplasms,[12] low frequency complications of the procedure may become more apparent. One such complication could be endocarditis.

In the most widely disseminated recommendations about antibiotic prophylaxis,[10] it was noted that lower GI tract procedures "have only rarely, *if ever,* been associated with the development of endocarditis," that valvular heart disease does not require prophylaxis, but that "since the patient with a prosthetic heart valve appears to be at especially high risk, it *may* be wise to administer antibiotic prophylaxis [emphasis added]" and that "this empiric recommendation is based more on concern than on definitive data."

In contrast, the majority of physicians in the Denver metropolitan area who would most likely be consulted about this problem (endoscopists, cardiologists and infectious disease specialists), are recommending antibiotic prophylaxis for all forms of valvular heart disease. We do not believe that the responses we obtained were strongly biased in favor of prophylaxis. On the questionnaire, "None" was presented as an equally acceptable choice and although a statement such as "To whom, if anyone, do you give antibiotic prophylaxis?" might have been more neutral, we wanted to be sure that those who were not cardiologists would address the issues of mitral valve prolapse and prosthetic valves. Whether the physicians' recommendations actually reflect their practice habits cannot be judged from this study. The basis for these recommendations is unclear. A recent survey of gastroenterology program directors[11] indicates that the majority are not giving antibiotic prophylaxis for lower GI tract procedures and are pre-

sumably teaching their fellows to approach the problem in the same way. It is possible that some physicians use prophylaxis because of a concern about possible litigation if endocarditis should develop. Most likely, however, these physicians have concluded that the risk of endocarditis is greater than the costs of giving antibiotics (particularly because most give less than the recommended three doses of antibiotics).

The actual risk of endocarditis developing following lower GI tract endoscopy in a patient who has valvular heart disease cannot be determined accurately. However, the absence of other cases being reported suggests that endocarditis must be rare, if not unique. There are several possible reasons for the rarity of this event. First, the 10% to 27% risk of bacteremia reported by some authors[1-3] is overstated. A more balanced overview of the studies[1-9] that have tried to document bacteremia occurring in such a circumstance is that bacteremia does occur, occurs infrequently, is transient and does not correlate well with surgical manipulation of, or disease in, the colon. Second, bacteria in the portal bloodstream are rapidly and effectively cleared by the hepatic reticuloendothelial system. This would decrease the number of bacteria reaching an abnormal valve. Of the enteric flora, however, the enterococci are highly adherent to endothelium in experimental models,[13] and thus the quantity of bacteria reaching the valve may be of lesser importance. Third, even after dental extractions, a more generally accepted cause of endocarditis, the risk of endocarditis developing when no prophylaxis is given is very small (1.1%).[14] Last, if practice habits across the country mimic those that are currently being recommended in our local survey, then a large portion of patients with valvular heart disease may be receiving antibiotic prophylaxis, which, if effective, might further reduce the risk of endocarditis. Of course, "initial" case reports may lead to corroborative letters of previously unreported cases that may suggest a greater risk. The true risk of endocarditis could be accurately assessed only by a large multicenter prospective study.

The costs (economic, morbidity and mortality) of antibiotic prophylaxis are more easily quantified. It is generally agreed that either ampicillin (1 gram given intramuscularly)—or vancomycin hydrochloride (1 gram given intravenously) in patients allergic to penicillin—and an aminoglycoside (gentamicin, 2 mg per kg of body weight given intramuscularly) are the antibiotics of choice.[10,15] The rationale for three doses of antibiotics (before procedure and at 8 and 16 hours) is that the second and third doses will kill bacteria that are adherent to the damaged epithelial surface. There is little experimental[16] and no clinical evidence that a multiple-dose regimen is more efficacious than a single dose before the procedure. The added cost of the antibiotics in our hospital pharmacy varies from $15 if one dose is given at the time of the procedure to $45 if three doses are given as an outpatient. The added cost of the three-dose regimen might make sigmoidoscopic screening for colorectal neoplasms[12] less cost effective. We have noted several outpatient colonoscopies changed to an inpatient procedure solely because the patient had valvular heart disease, resulting in further costs. The risk of nonfatal drug reactions is about 9% (mostly skin rashes, assuming that three doses of an aminoglycoside have a negligible risk of compromising renal function), and the risk of fatal anaphylaxis from a penicillin is 1 in 50,000.[17] Indeed, if endocarditis is extremely rare, the antibiotic prophylaxis may carry more risk than what it is trying to prevent.

In our view, this case of enterococcal endocarditis following a flexible sigmoidoscopy provides the first clear evidence that there is a finite risk from bacteremia after lower GI tract endoscopy. This strengthens the contention that antibiotic prophylaxis should be used in those clinical situations wherein the consequences of bacteremia would be so devastating that even the remote chance of distant infection could not be tolerated.[10,15] In addition to those who have prosthetic heart valves, we would also give prophylaxis to patients with artificial joints, those on hemodialysis who have arteriovenous shunts and patients who are severely neutropenic, the last because of the risk of septicemia. Until a large prospective study can be undertaken to address this issue, however, the apparent rarity of endocarditis occurring postlower GI tract procedure does not appear to justify the expense and morbidity entailed in administering three doses of antibiotic prophylaxis to all patients who have acquired or congenital valvular disease.

Addendum

Since submission of this article, Rigilano and coworkers reported a case of enterococcal endocarditis occurring after rigid sigmoidoscopy.[18] Their suggestion that flexible instruments may have a lower risk for this complication is weakened by our report.

REFERENCES

1. LeFrock JL, Ellis CA, Turchik JB, et al: Transient bacteremia associated with sigmoidoscopy. N Engl J Med 1973 Aug; 289:467-469
2. Pelican G, Hentges D, Butt J, et al: Bacteremia during colonoscopy. Gastrointest Endosc 1976 Aug; 23:33-35
3. Liebermann TR: Bacteremia and fiberoptic endoscopy. Gastrointest Endosc 1976 Aug; 23:36-37
4. Kumar S, Abcarian H, Prasad ML, et al: Bacteremia associated with lower gastrointestinal endoscopy, fact or fiction? I. Colonoscopy. Dis Colon Rectum 1982 Mar; 25:131-134
5. Dickman MD, Farrell R, Higgs RH, et al: Colonoscopy associated bacteremia. Surg Gynecol Obstet 1976 Feb; 142:173-176
6. Norfleet RG, Mulholland DD, Mitchell PD, et al: Does bacteremia follow colonoscopy? Gastroenterology 1976 Jan; 70:20-21
7. Coughlin GP, Butler RN, Alp MH, et al: Colonoscopy and bacteremia. Gut 1977 Aug; 18:678-679
8. Hartong WA, Barnes WG, Calkins WG: The absence of bacteremia during colonoscopy. Am J Gastroenterol 1977 Mar; 67:240-244
9. Engeling ER, Eng BF, Sullivan-Sigler N, et al: Bacteremia after sigmoidoscopy—Another view (Letter). Ann Intern Med 1976 Jul; 85: 77-78
10. Kaplan EL, Anthony BF, Bisno A, et al: AHA Committee Report—Prevention of bacterial endocarditis. Circulation 1977 Jul; 56:139A-143A
11. Meyer GW: Prophylaxis of infective endocarditis during gastrointestinal procedures: Report of a survey. Gastrointest Endosc 1979 Jan; 25:1-2
12. Winawer SJ, Sherlock P, Schottenfeld D, et al: Screening for colon cancer. Gastroenterology 1976 May; 70:783-789
13. Gould K, Ramirez-Ronda CH, Holmes RK, et al: Adherence of bacteria to heart valves in vitro. J Clin Invest 1975 Dec; 56:1364-1370
14. Taran LM: Rheumatic fever in its relation to dental disease. NY J Dent 1944 Mar; 14:107-113
15. Everett ED, Hirschmann JV: Transient bacteremia and endocarditis prophylaxis. Medicine (Baltimore) 1977 Jan; 56:61-77
16. Pelletier LL Jr, Durack DT, Petersdorf RG: Chemotherapy of experimental streptococcal endocarditis—IV. Further observations on prophylaxis. J Clin Invest 1975 Aug; 56:319-330
17. Idsoe O, Guthe T, Willcox RR, et al: Nature and extent of penicillin side-reactions, with particular reference to fatalities from anaphylactic shock. Bull WHO 1968 Aug; 38:159-188
18. Rigilano J, Mahapatra R, Barnhill J, et al: Enterococcal endocarditis following sigmoidoscopy and mitral valve prolapse. Arch Intern Med 1984; 144:850-851